AUG 2 8 2006

Serial No.: 10/527,561 Case No.: 21204P Page No.:

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the present application.

Listing of Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claim 1. (currently amended) A compound of structural formula I:

$$R^3$$
 R^2
 N
 R^1

or a pharmaceutically acceptable salt thereof, wherein:

R1 is selected from:
——————————————————————————————————————
- (2) OR*,
$\frac{\text{(3)}}{\text{NReRb}},$
(4)NR ^b C(O)R#,
- (5) CO2Ra,
——————————————————————————————————————
——————————————————————————————————————
(8) SO2Rb,
(1) <u>C₁₋₆alkyl</u> ,

- (2) -OH,
- (3) -OC1-6alkyl, unsubstituted or substituted with one to three RC substituents,
- (4) cycloalkyloxy-, unsubstituted or substituted with one to three Rc substituents,
- (5) cycloalkyl-C1-4alkyloxy-, unsubstituted or substituted with one to three RC substituents,
- (6) cycloheteroalkyloxy-, unsubstituted or substituted with one to three Rc substituents,
- (7) cycloheteroalkyl-C1_4 alkyloxy, unsubstituted or substituted with one to three RC substituents,
- (8) phenyloxy, unsubstituted or substituted with one to three R^o substituents,
- (9) heteroaryloxy, unsubstituted or substituted with one to three Rc substituents,
- (10) phenyl-C1-4alkyloxy, unsubstituted or substituted with one to three Rc substituents,

Serial No.: 10/527,561 Case No.: 21204P

Page No.: 3

- (11) heteroaryl-C₁₋₄alkyloxy, unsubstituted or substituted with one to three R^c substituents,
- (12) -NRaRb.
- (13) -NRbC(O)Ra.
- (14) -CO₂H,
- (15) C₁₋₆alkyloxycarbonyl-, unsubstituted or substituted with one to three R^c substituents,
- (16) cycloalkyloxycarbonyl-, unsubstituted or substituted with one to three RC substituents,
- (17) cycloalkyl-C₁₋₄alkyloxycarbonyl-, unsubstituted or substituted with one to three R^c substituents.
- (18) phenyloxycarbonyl, unsubstituted or substituted with one to three RC substituents,
- (19) heteroaryloxycarbonyl, unsubstituted or substituted with one to three RC substituents,
- (20) phenyl-C₁_4alkyloxycarbonyl, unsubstituted or substituted with one to three R^c substituents,
- (21) heteroaryl-C1-4alkyloxycarbonyl, unsubstituted or substituted with one to three RC substituents,
- (22) -C(O)NRaRb.
- (23) cyano,
- (24) -SO₂C₁-6alkyl, unsubstituted or substituted with one to three RC substituents; and provided that R¹ is not -NH₂;

R² is selected from:

- (1) hydrogen,
- (2) C₁₋₁₀alkyl,
- (3) -ORa,
- (4) -NRaRb,
- (5) -NRaC(O)Rb,
- (6) -CO₂Ra,
- (7) -C(O)NRaRb,
- (8) cyano,
- (9) -SRa, and
- (10) $-SO_2R^2$;

wherein R³ and R⁴ are each independently selected from:

each Ra is independently selected from:

- (1) hydrogen,
- (2) C₁₋₁₀alkyl,
- (3) C2-10 alkenyl,
- (4) cycloalkyl,
- (5) cycloalkyl-C₁₋₁₀alkyl;
- (6) cycloheteroalkyl,
- (7) cycloheteroalkyl-C_{I-10} alkyl;
- (8) aryi,
- (9) heteroaryl,
- (10) aryl-C1-10alkyl, and
- (11) heteroaryl-C1-10alkyl; and

each R^{b} is independently selected from:

- (1) hydrogen,
- (2) C_{1-10} alkyl,
- (3) C2-10 alkenyl,
- (4) cycloalkyl,
- (5) cycloalkyl-C₁₋₁₀alkyl;
- (6) cycloheteroalkyl,
- (7) cycloheteroalkyl-C₁₋₁₀ alkyl;
- (8) aryl,

- (9) heteroaryl,
- (10) aryl-C1-10alkyl, and
- (11) heteroaryl-C1-10alkyl, or

R^a and R^b together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-R^d,

each Ra and Rb may be unsubstituted or substituted with one to three substituents selected from Rc; each Rc is independently selected from:

- (1) C₁₋₁₀alkyl,
- (2) -ORd,
- (3) $-NReS(O)_mRd$
- (4) halogen,
- (5) -SRd,
- (6) $-S(O)_mNRdRe$,
- (7) -NRdRe,
- (8) -C(O)Rd
- (9) -CO₂Rd,
- (10) -CN,
- (11) -C(O)NRdRe,
- (12) $-NR^{\varrho}C(Q)R^{d}$,
- (13) -NRCC(O)ORde,
- (14) -NReC(O)NRdRe,
- (15) -CF3,
- (16) -OCF3,
- (17) cycloheteroalkyl,
- (18) aryl,
- (19) arylC_{1-4alkyl},
- (20) heteroaryl, and
- (21) heteroaryiC1.4alkyl;

Rd and Re are independently selected from:

- (1) hydrogen,
- (2) C₁₋₁₀alkyl,
- (3) C_{2-10} alkenyl,
- (4) cycloalkyl,
- (5) cycloalkyl-C1-10alkyl;
- (6) cycloheteroalkyi,

AUG-28-2006 17:00 P.07

Serial No.: 10/527,561 Case No.: 21204P Page No.: 6

- (7) cycloheteroalkyl-C₁₋₁₀ alkyl;
- (8) aryl,
- (9) heteroaryl,
- (10) aryi-C1-10alkyi, and
- (11) heteroaryl-C1-10alkyl, or

Rd and Re together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-Rf,

each R^d and R^c may be unsubstituted or substituted with one to three substituents selected from R^f ; R^f is independently selected from:

- (1) halogen,
- (2) C₁₋₁₀alkyl,
- (3) -O-C₁₋₄alkyl,
- (4) -S-C1-4alkyl,
- (5) -CN,
- (6) -CF3, and
- (7) -OCF3;

each RS is independently selected from:

- (1) halogen,
- (2) C₁₋₁₀alkyl,
- (3) -O-C1-4alkyl,
- (4) -S-C₁₋₄alkyl,
- (5) -CN,
- (6) -CF3, and
- (7) -OCF3; and

m is selected from 1 and 2.

Claim 2. (canceled)

Claim 3. (canceled)

Claim 4. (currently amended) The compound according to Claim 1, wherein:

R1 is selected from:

- (1) C1 6alkyl,
- (2) OH,
- (3) OC1-6alkyl, unsubstituted or substituted with one to three Ro substituents,

AUG-28-2006 17:00 P.08

- (4) cycloalkyloxy, unsubstituted or substituted with one to three R6 substituents,
- (5) eyoloalkyl G1_4alkyloxy , unsubstituted or substituted with one to three R6 substituents;
- (6) cycloheteroalkyloxy, unsubstituted or substituted with one to three Ro substituents,
- (7)—eyelohoteroalkyl C₁ 4 alkylexy, unsubstituted or substituted with one to three Resubstituents;
- (8) phenyloxy, unsubstituted or substituted with one to three Ro substituents.
- (9) heteroarylexy, unsubstituted or substituted with one to three Re substituents,
- (10) phonyl-G1_4alkyloxy, unsubstituted or substituted with one to three RC substituents.
- (11) heteroaryl C₁_4alkyloxy, unsubstituted or substituted with one to three R⁰ substituents,
- (12) NRaRb.
- (13) NR+C(O)Ra.
- (14) CO2H,
- (15) C1 6alkyloxycarbonyl, unsubstituted or substituted with one to three R0 substituents,
- (16) cycloalkyloxycarbonyl, unsubstituted or substituted with one to three R6 substituents.
- (17)—cycloalkyl-G_{1-4alkyloxycarbonyl}, unsubstituted or substituted with one to three Resubstituents,
- (18) phenyloxycarbonyl, unsubstituted or substituted with one to three Re substituents,
- (19) heteroaryloxyearbonyl, unsubstituted or substituted with one to three R6 substituents,
- (20) phenyl-C1 4alkylexyearbonyl, unsubstituted or substituted with one to three Resubstituents,
- (21) heteroaryl-G₁.4alkyloxyearbonyl, unsubstituted or substituted with one to three R^c substituents:
- (22) -- C(O)NRaRb,
- (23) cyano,
- (24) SO₂G₁₋₆alkyl, unsubstituted or substituted with one-te-three Re-substituents; and Ra and Rb are each selected from:
 - (1) hydrogen,
 - (2) C1-6alkyl, unsubstituted or substituted with one to three RC substituents,
 - (3) cycloalkyl, unsubstituted or substituted with one to three Rc substituents,
 - (4) cycloalkyl-C1-4alkyl, unsubstituted or substituted with one to three Rc substituents,
 - (5) phenyl, unsubstituted or substituted with one to three RC substituents,
 - (6) heteroaryl, unsubstituted or substituted with one to three RC substituents,
 - (7) phenyl-C1-4alkyl, unsubstituted or substituted with one to three Rc substituents, or

Serial No.: 10/527,561 Case No.: 21204P

Page No.:

(8) heteroaryl-C₁-4alkyl, unsubstituted or substituted with one to three R^c substituents, or when bonded to nitrogen, R^a and R^b together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-Rd, unsubstituted or substituted on carbon with one to three R^c substitutents;

or a pharmaceutically acceptable salts thereof.

Claim 5. (currently amended) The compound according to Claim 4, wherein R1 is selected from:

- (1) (1) C₁₋₆alkyl,
- (2) OH,
- (3) (2) OC1-6alkyl, unsubstituted or substituted with one to three Rc substituents,
- (4) (3) C4-7cycloalkyloxy-, unsubstituted or substituted with one to two Rc substituents,
- (5) (4) cycloalkyl-C₁₋₃alkyloxy-, unsubstituted or substituted with one to two Rc substituents,
- (6) (5) phenyloxy, unsubstituted or substituted with one to two Rc substituents,
- (7) (6) pyridyloxy, unsubstituted or substituted with one to two R^c substituents,
- (8) (7) phenyl-C1-3alkyloxy, unsubstituted or substituted with one to two RC substituents,
- (9) (8) pyridyl-C₁₋₃alkyloxy, unsubstituted or substituted with one to two R^c substituents,
- (10) (9) -NRaRb, wherein:

Ra is selected from:

- (a) C1-6alkyl, unsubstituted or substituted with one to three Rc substituents,
- (b) cycloalkyl, unsubstituted or substituted with one to two Rc substituents,
- (c) cycloalkyl-C₁_4alkyl, unsubstituted or substituted with one to two R^c substituents,
- (d) phenyl, unsubstituted or substituted with one to two Rc substituents,
- (e) heteroaryl, unsubstituted or substituted with one to two Rc substituents,
- (f) benzyl, unsubstituted or substituted with one to two R^c substituents, R^b is selected from:
- (a) hydrogen,
- (b) C₁-6alkyl, unsubstituted or substituted with one to three R^c substituents, or R^a and R^b together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-Rd, unsubstituted or substituted on carbon with one to two R^c substitutents,

Serial No.: 10/527,561 Case No.: 21204P

Page No.:

(11) (10) -NRbC(O)Ra, wherein:

Ra is selected from:

- (a) hydrogen,
- (b) C1-6alkyl, unsubstituted or substituted with one to three Rc substituents,
- (c) cycloalkyl, unsubstituted or substituted with one to two Rc substituents,
- (d) cycloalkyl-C1_4alkyl, unsubstituted or substituted with one to two Rc substituents,
- (e) phenyl, unsubstituted or substituted with one to two RC substituents,
- (f) pyridyl, unsubstituted or substituted with one to three Rc substituents,
- (g) benzyl, unsubstituted or substituted with one to two RC substituents,
- (h) pyridylmethyl-, unsubstituted or substituted with one to three Rc substituents,

Rb is selected from:

- (a) hydrogen,
- (b) C_{1-6alkyl}, unsubstituted or substituted with one to three R^c substituents,
- (12) (11) -CO₂H,
- (13) (12) C1-6alkyloxycarbonyl-, unsubstituted or substituted with one to three RC substituents,
- (14) (13) -C(O)NRaRb, wherein:

Ra is selected from:

- (a) hydrogen,
- (b) C₁-6alkyl, unsubstituted or substituted with one to three Rc substituents,

Rb is selected from:

- (a) hydrogen, and
- (b) C₁₋₆alkyl, unsubstituted or substituted with one to three R^c substituents,
- (15) (14) cyano
- (16) (15) -SC1-6alkyl, unsubstituted or substituted with one to three Rc substituents, and
- (17) (16) -SO₂C₁-6alkyl, unsubstituted or substituted with one to three RC substituents; each RC is independently selected from:
 - (1) C₁₋₃alkyl,
 - (2) hydroxy,
 - (3) $-OC_{1-3}$ alkyl,
 - (4) halogen,
 - (5) -SCH3,
 - (6) -SH,
 - (7) -NRdRe.
 - (8) $-C(O)C_{1-3}alkyl$

- (9) -CO2C1-3alkyl,
- (10) -CO₂H,
- (11) -CN,
- (12) -CF3,
- (13) -OCF3,
- (14) cycloheteroalkyl,
- (15) phenyl,
- (16) benzyl, and
- (17) pyridyl;

or a pharmaceutically acceptable salts thereof.

Claim 6. (previously presented) The compound according to Claim 4, wherein R2 is selected from:

- (1) hydrogen,
- (2) C₁₋₆alkyl,
- (3) -OH,
- (4) -OC1-6alkyl, unsubstituted or substituted with one to three R^c substituents,
- (5) cycloalkyloxy-, unsubstituted or substituted with one to three Rc substituents,
- (6) cycloalkyl-C₁-4alkyloxy-, unsubstituted or substituted with one to three RC substituents,
- (7) cycloheteroalkyloxy-, unsubstituted or substituted with one to three Rc substituents,
- (8) cycloheteroalkyl-C1-4 alkyloxy, unsubstituted or substituted with one to three Rc substituents,
- (9) phenyloxy, unsubstituted or substituted with one to three Rc substituents,
- (10) heteroaryloxy, unsubstituted or substituted with one to three Rc substituents,
- (11) phenyl-C1-4alkyloxy, unsubstituted or substituted with one to three RC substituents,
- (12) heteroaryl-C1_4alkyloxy, unsubstituted or substituted with one to three Rc substituents,
- (13) -NRaRb.
- (14) -NRbC(Q)Ra,
- (15) -CO₂H,
- (16) C1-6alkyloxycarbonyl-, unsubstituted or substituted with one to three RC substituents,
- (17) cycloalkyloxycarbonyl-, unsubstituted or substituted with one to three RC substituents.
- (18) cycloalkyl-C₁₋₄alkyloxycarbonyl-, unsubstituted or substituted with one to three R¢ substituents,

AUG-28-2006 17:01 P.12

Serial No.: 10/527,561 Case No.: 21204P Page No.: 11

- (19) phenyloxycarbonyl, unsubstituted or substituted with one to three Rc substituents,
- (20) heteroaryloxycarbonyl, unsubstituted or substituted with one to three R¢ substituents,
- (21) phenyl-C₁₋₄alkyloxycarbonyl, unsubstituted or substituted with one to three Rc substituents,
- (22) heteroaryl-C₁-4alkyloxycarbonyl, unsubstituted or substituted with one to three R^c substituents,
- (23) -C(O)NRaRb,
- (24) cyano,
- (25) -SC1-6alkyl, unsubstituted or substituted with one to three RC substituents, and
- (26) -SO₂C₁₋₆alkyl, unsubstituted or substituted with one to three R^c substituents, or a pharmaceutically acceptable salts thereof.

Claim 7. (previously presented) The compound according to Claim 1, wherein: \mathbb{R}^2 is selected from:

- (1) hydrogen,
 - (2) C1-6alkyl,
 - (3) -OH,
 - (4) -OC1-6alkyl, unsubstituted or substituted with one to three Rc substituents,
 - (5) C4-7cycloalkyloxy-, unsubstituted or substituted with one to two R^c substituents,
 - (6) C4-7cycloalkyl-C1-3alkyloxy-, unsubstituted or substituted with one to two Rc substituents,
 - (7) phenyloxy, unsubstituted or substituted with one to two RC substituents,
 - (8) pyridyloxy, unsubstituted or substituted with one to two Rc substituents,
 - (9) phenyl-C1-3alkyloxy, unsubstituted or substituted with one to two RC substituents,
 - (10) pyridyl-C1-3alkyloxy, unsubstituted or substituted with one to two RC substituents,
 - (11) -NRaRb, wherein:

Ra is selected from:

- (a) hydrogen,
- (b) C₁₋₆alkyl, unsubstituted or substituted with one to three Rc substituents,
- (c) cycloalkyl, unsubstituted or substituted with one to two RC substituents,
- (d) cycloalkyl-C₁-4alkyl, unsubstituted or substituted with one to two Rc substituents,
- (e) phenyl, unsubstituted or substituted with one to two RC substituents,
- (f) heteroaryl, unsubstituted or substituted with one to two RC substituents,
- (g) benzyl, unsubstituted or substituted with one to two RC substituents,

Rb is selected from:

- (a) hydrogen,
- (b) C₁-6alkyl, unsubstituted or substituted with one to three R^c substituents, or R^a and R^b together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members, unsubstituted or substituted on carbon with one to two R^c substitutents,
- (12) -NHC(O)Ra, wherein:

Ra is selected from:

- (a) hydrogen,
- (b) C1-6alkyl, unsubstituted or substituted with one to three Rc substituents,
- (c) cycloalkyl, unsubstituted or substituted with one to two Rc substituents,
- (d) cycloalkyl-C₁₋₄alkyl, unsubstituted or substituted with one to two R^c substituents,
- (e) phenyl, unsubstituted or substituted with one to two Rc substituents,
- (f) pyridyl, unsubstituted or substituted with one to three R^c substituents,
- (g) benzyl, unsubstituted or substituted with one to two RC substituents,
- (h) pyridylmethyl-, unsubstituted or substituted with one to three R^c substituents.
- (13) cyano, and
- (14) -SO₂C₁-6alkyl, unsubstituted or substituted with one to three R^c substituents; or a pharmaceutically acceptable salts thereof.

Claim 8. (currently amended) The compound according to Claim 1, wherein: R1 is selected from:

- (1) methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert.-butyl, n-pentyl, or 2,2-dimethylpropyloxy,
- —— (2) OH.
 - (3)(2) methoxy, ethyloxy, isopropyloxy, n-butyloxy, sec-butyloxy, isobutyloxy, tert.-butyloxy, n-pentyloxy, or 2,2-dimethylpropyloxy, unsubstituted or substituted with one to three halo, hydroxy, or methoxy substituents,
 - (4)(3) cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, or cycloheptyloxy,
 - (5)(4) cyclopropylmethoxy, cyclobutylmethoxy, cyclopentylmethoxy, cyclohexylmethoxy, or cycloheptylmethoxy,
 - (6)(5) 4-fluorophenyloxy, 4-chlorophenyloxy, 4-methoxyphenyloxy, 3-fluorophenyloxy, 3-chlorophenyloxy, 3,4-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy,

AUG-28-2006 17:01 P.14

Serial No.: 10/527,561 Case No.: 21204P Page No.: 13

(7) (6) 4-pyridyloxy, 3-pyridyloxy, 6-chloro-3-pyridyloxy, or 5-chloro-3-pyridyloxy,

(8)(7) benzyloxy, 3-fluorobenzyloxy, 3-chlorobenzyloxy, 4-fluorobenzyloxy, 4-chlorobenzyloxy, 3,4-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 2,4-fluorobenzyloxy, 2,4-dichlorobenzyloxy, alpha-methyl-4-fluorobenzyloxy, or alpha,alpha-dimethyl-4-chlorobenzyloxy,

(9)(8) 2-pyridylmethyloxy 3,-pyridylmethyloxy, or 4-pyridylmethyloxy,
(10)(9) N-methylamino, N,N-dimethyamino, N,N-diisopropylamino, or
N(CH3)CH2CH2N(CH3)2, or N-containing heterocycloalkyl bonded via nitrogen selected
from: morpholinyl, thiomorpholinyl, pyrrolidinyl, piperidinyl, and [2.2.1]azabicycloheptyl,

(11)(10) -NHCORa wherein Ra is selected from:

- (a) hydrogen,
- (b) C₁₋₄alkyl,
- (c) C4-6cycloalkyl, and
- (d) phenyl, 4-fluorophenyl, 4-chlorophenyl, 3,4-difluorophenyl, or 3,4-

dichlorophenyl,

(12)(11) -CO₂H, (13)(12) -C(O)NH₂, (14)(13) -CN, and (15)(14) -SO₂CH₃:

R² is selected from:

- (1) hydrogen,
- (2) methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert.-butyl, n-pentyl, or 2,2-dimethylpropyloxy,
- (3) -OH,
- (4) methoxy, ethyloxy, isopropyloxy, n-butyloxy, sec-butyloxy, isobutyloxy, tert.-butyloxy, n-pentyloxy, or 2,2-dimethylpropyloxy, unsubstituted or substituted with one to three halo, hydroxy, or methoxy substituents,
- (5) cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, or cycloheptyloxy,
- (6) cyclopropylmethoxy, cyclobutylmethoxy, cyclopentylmethoxy, cyclohexylmethoxy, or cycloheptylmethoxy,
- (7) 4-fluorophenyloxy, 4-chlorophenyloxy, 3-fluorophenyloxy, 3-chlorophenyloxy, 3-chlorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy, or phenyloxy,

- (8) benzyloxy, 3-fluorobenzyloxy, 3-chlorobenzyloxy, 4-fluorobenzyloxy, 4-chlorobenzyloxy, 3,4-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 2,4-fluorobenzyloxy, or 2,4-dichlorobenzyloxy,
- (9) 4-pyridyloxy, 3-pyridyloxy, 6-chloro-3-pyridyloxy, or 5-chloro-3-pyridyloxy,
- (10) amino, N-methylamino, N-ethylamino, N,N-dimethyamino, N,N-diethylamino,N,N-diisopropylamino, or N-containing heterocycloalkyl bonded via nitrogen selected from: pyrrolidinyl, and piperidinyl,
- (11) -NHCORa wherein Ra is selected from:
 - (a) hydrogen, and
 - (b) C_{1-4alkyl},
- (12) -CN, and
- (13) $-SO_2CH_3$;

R3 and R4 are each independently selected from:

- (1) 4-chlorophenyl,
- (2) 4-methoxyphenyl,
- (3) 4-fluorophenyl,
- (4) 4-trifluoromethylphenyl,
- (5) 3-chlorophenyl,
- (6) 3-methoxyphenyl,
- (7) 2,4-dichlorophenyl, and
- (8) 2-chloro-4-methylthiophenyl;

or a pharmaceutically acceptable salts thereof.

Claim 9. (previously presented) The compound according to Claim 8, wherein:

R³ is 4-chlorophenyl and R⁴ is 2,4-dichlorophenyl, or a pharmaceutically acceptable salt thereof.

Claim 10 (canceled)

Claim 11. (currently amended) A method of treating a disease mediated by the Cannabinoid-1 receptor selected from: psychosis, memory deficit, cognitive disorders, migraine, neuropathy, neuro-inflammatory-disorders, corebral vascular accidents, head-trauma, anxiety disorders, stress, epilepsy, Parkinson's disease, sohizophrenia, substance abuse disorders, constipation, chronic intestinal pseudo-obstruction, citrhosis of the liver, asthma, obesity, and other cating disorders associated with excessive food intake, comprising administration to a patient in need of such

treatment of a therapeutically effective amount of a compound according to Gleim 1 compound of structural formula I:

$$R^3$$
 R^2
 N
 R^1

(I)

or a pharmaceutically acceptable salt thereof, wherein:

R1 is selected from:

- (1) C_{1-10alkyl}
 - (2) -ORa,
- (3) -NRaRb,
- ____(4) -NRbC(O)Ra,
- ____(5) -CO₂Ra,
- (6) -C(O)NRaRb
- _____(7) cyano, and
- _____(8) _SO₂Rb,

provided that R1 is not -NH2:

R2 is selected from:

- (1) hydrogen,
- (2) <u>C_{1-10alkyl}</u>,
- (3) -ORa,
- (4) -NRaRb
- (5) -NRaC(O)Rb,
- (6) -CO2R2,
- (7) -C(O)NRaRb
- (8) cyano,
- (9) -SRa, and
- (10) -SO₂Ra;

wherein R3 and R4 are each independently selected from:

<u>(1)</u>

$$\mathbb{R}^{g}$$

(3)

 $\begin{array}{c} (4) \\ \hline \\ N \end{array}$

each Ra is independently selected from:

- (I) hydrogen,
- (2) C1-10alkyl.
- (3) C2-10 alkenyl.
- (4) cycloalkyl,
- (5) cycloalkyl-C1-10alkyl;
- (6) cycloheteroalkyl,
- (7) cycloheteroalkyl-C1-10 alkyl:
- (8) aryl,
- (9) heteroaryl,
- (10) aryl-C1-10alkyl, and
- (11) heteroaryl-C1-10alkyl; and

each Rb is independently selected from:

- (1) hydrogen,
- (2) <u>C₁₋₁₀alkyl</u>,
- (3) <u>C2-10 alkenyl</u>
- (4) cycloalkyl,
- (5) cycloalkyl-C1-10alkyl;
- (6) cycloheteroalkyl,
- (7) cycloheteroalkyl-C1-10 alkyl;
- (8) aryl,
- (9) heteroaryl,
- (10) aryl-C1-10alkyl, and
- (11) heteroaryl-C1-10alkyl, or

Ra and Rb together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-Rd.

each Ra and Rb may be unsubstituted or substituted with one to three substituents selected from Rc; each Rc is independently selected from:

- (1) C_{1-10} alkyl,
- (2) -ORd,
- $(3) -NReS(O)_mRd,$
- (4) halogen,
- (5) -SRd.
- (6) -S(O)mNRdRe
- (7) -NRdRe,
- (8) -C(O)Rd
- (9) <u>-CO₂Rd</u>
- (10) -CN,
- (11) -C(O)NRdRe.
- (12) -NReC(O)Rd
- (13) -NReC(O)ORde,
- (14) -NRC(O)NRdRe,
- (15) -CF3.
- (16) -OCF3,
- (17) cycloheteroalkyl,
- (18) aryl,
- (19) arylC₁ 4alkyl,
- (20) heteroaryl, and
- (21) heteroaryiC1_4alkyl;

Rd and Re are independently selected from:

- (1) hydrogen,
- (2) C1-10alkyl.
- (3) C2-10 alkenyl.
- (4) cycloalkyl,
- (5) cycloalkyl-C1-10alkyl:
- (6) cycloheteroalkyl,
- (7) cycloheteroalkyl-C1-10 alkyl:
- (8) aryl,
- (9) heteroaryl,

- (10) aryl-C1-10alkyl, and
- (11) heteroaryl-C1-10alkyl, or

Rd and Re together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-Rf.

each Rd and Re may be unsubstituted or substituted with one to three substituents selected from Rf. Rf is independently selected from:

- (1) halogen,
- (2) <u>C1-10alkyl</u>,
- (3) -O-C1-4alkyl,
- (4) -S-C_{1-48lkyl}
- (5) -CN,
- (6) -CF3, and
- (7) -OCF3;

each Rg is independently selected from:

- (1) halogen,
- (2) <u>C1-10alkyl</u>,
- (3) <u>-O-C</u>_{1-42lkyl},
- (4) <u>-S-C1-4alkyl.</u>
- (5) -CN.
- (6) -CF3 and
- (7) -OCF3: and

m is selected from 1 and 2.

Claim 12. (canceled)

Claim 13. (previously presented)

The method according to Claim 11 wherein the disease mediated by the Cannabinoid-1 receptor is an eating disorder associated with excessive food intake.

Claim 14. (currently amended) The method according to Claim 13 wherein the cating disorder associated associated with excessive food intake is selected from obesity, bulimia nervosa, and compulsive eating disorders.

Claim 15. (original) The method according to Claim 14 wherein the eating disorder associated with excessive food intake is obesity.

AUG-28-2006 17:02 P.20

Serial No.: 10/527,561 Case No.: 21204P Page No.: 19

Claim 16. (cancelled)

Claim 17. (original) A composition comprising a compound according to Claim 1 and a pharmaceutically acceptable carrier.

Claims 18-24 (cancelled)

Claim 25. (currently amended) The method according to Claim 11 for treating substance abuse disorders, wherein the abused substance is nicotine in a person dependent on nicotine; comprising administering a therapeutically effective amount of a compound according to Claim 1 to the person.

Claim 26. (new) The compound according to Claim 1, selected from:

- (1) 2-(4-fluorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (2) 2-(4-fluorobenzyloxy)-4-(2-chloro-4-methylthiophenyl)-5-(4-chlorophenyl)-pyrimidine;
- (3) 2-(3,4-difluorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (4) 2-(3,4-difluorobenzyloxy)-4-(2-chloro-4-methylthio-phenyl)-5-(4-chlorophenyl)-pyrimidine;
- (5) 2-(4-chlorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (6) 2-(4-chlorobenzyloxy)-4-(2-chloro-4-methylthio-phenyl)-5-(4-chlorophenyl)-pyrimidine;
- (7) 2-(3,4-dichlorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (8) 2-(3,4-dichlorobenzyloxy)-4-(2-chloro-4-methylthio-phenyl)-5-(4-chlorophenyl)-pyrimidine;
- (9) 2-(3-fluorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (10) 2-(3-fluorobenzyloxy)-4-(2-chloro-4-methylthio-phenyl)-5-(4-chlorophenyl)-pyrimidine;
- (11) 2-(3-chlorobenzylamino)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-pyrimidine;
- (12) 2-(N,N-dimethylamino)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (13) 2-carboxy-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (14) 2-methoxy-4-hydroxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (15) 2-(3,4-difluorobenzyloxy)-4-hydroxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (16) 2-(3,4-difluorobenyloxy)-4-hydroxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (17) 2,4-bis-(3,4-difluorobenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (18) 2,4-dimethoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (19) 2,4-dicthoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (20) 2,4-diisopropoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (21) 2-methylsulfonyl-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;

- (22) 2,4-bis(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (23) 2-cyano-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (24) 2-(3,4-difluorobenzyloxy)-4-cyano-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (25) 2-cyano-4-(3,4-difluorobenzyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (26) 2,4-bis(cyano)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (27) 2-(3,4-difluorophenoxy)-4-methyl-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (28) 2-ethyl-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (29) 2-isopropy-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (30) 2-(3,4-difluorobenzyloxy)-4-methyl-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (31) 2-(3,4-difluorobenzyloxy)-4-ethyl-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (32) 2-(3,4-difluorobenzyloxy)-4-(N-methylamino)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (33) 2-(3,4-difluorophenoxy)-4-amino-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (34) 2-(3,4-difluorobenzyloxy)-4-(amino)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (35) 2-(3,4-difluorophenoxy)-4-(acetylamino)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (36) 2-(3,4-difluorobenzyloxy)-4-(acetylamino)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (37) 2-(3,4-difluorophenoxy)-4-(N-pytrolidinyl)-5-[4-chlorophenyl]-6-[2,4-dichlorophenyl]
- (38) 2-(cyclopropylmethoxy)-4-(N-pyrrolidinyl)-5-[4-chlorophenyl]-6-[2,4-dichlorophenyl] pyrimidine;
- (39) 2-(N,N-diethylamino)-4-(3,4-difluorobenzyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (40) 2-(N,N-diisopropylamino)-4-(3,4-difluorobenzyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (41) 2-(N-pyrrolidinyl)-4-(3,4-difluorobenzyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (42) 2-(N-piperidyl)-4-(3,4-difluorobenzyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (43) 2-(N-morpholinyl)-4-(3,4-difluorobenzyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (44) 2-(7-N-[2.2.1]-azabicycloheptyl)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (45) 2-(n-propionyl)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;

- (46) 2-(N-(2-methyl)propionyl)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (47) 2-(N-(3-methyl)butyryl)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (48) 2-(aminocarbonyl)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (49) 2-(carboxy)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (50) 2-(2-hydroxyethyleneoxy)-4-(3,4-difluorophcnoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (51) 2-(2-methoxyethyleneoxy)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (52) 2-(cyclohexylmethyloxy)-4-isopropoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (53) 2-cyclohexyloxy-4-isopropoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (54) 2-(3,4-difluorophenoxy)-4-cyclohexyloxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (55) 2-(3,4-diffuorobenzyloxy)-4-cyclohexyloxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (56) 2,4-bis(cyclopropylmethyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (57) 2-cyclopropyloxy-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (58) 2-(N-pyrrolidinyl)-4-cyclopropyloxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (59) 2,4-bis(isopropyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (60) 2-(3,4-difluorobenzyloxy)-4-(4-chlorophenyl)-5-(2,4-dichlorophenyl)pyrimidine;
- (61) 2-(4-chlorobenzyloxy)-4-(4-chlorophenyl)-5-(2,4-dichlorophenyl)pyrimidine;
- (62) 2-(3-fluorobenzyloxy)-4-(4-chlorophenyl)-5-(2,4-dichlorophenyl)pyrimidine;
- (63) 2-(3-chlorobenzyloxy)-4-(4-chlorophenyl)-5-(2,4-dichlorophenyl)pyrimidine;
- (64) 2-(4-fluorobenzyloxy)-4-(4-chlorophenyl)-5-(2,4-dichlorophenyl)pyrimidine;
- (65) 2-(α-methyl-4-fluorobenzyloxy-)-4-(4-chlorophenyl)-5-(2,4-dichlorophenyl)pyrimidine;
- (66) 2-(α-methyl-4-fluorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (67) 2-(3-pyridylmethoxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (68) 2-(n-butyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (69) 2-(2,4-dichlorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (70) 2-(cyclohexylmethoxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (71) 2-(3,5-dichlorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (72) 2-(6-chloro-3-pyridylmethoxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (73) 2-(α,α-dimethyl-4-fluorobenzyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (74) 2-(4-fluorophenyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;

- (75) 2-(3-fluorophenyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (76) 2-(3,4-difluorophenyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (77) 2-(3-chlorophenyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (78) 2-(4-methoxyphenyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (79) 2-(3-pyridyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (80) 2-(5-chloro-3-pyridyloxy)-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (81) 2-(N-(4-fluorobenzamido))-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (82) 2-(N-(cyclohexylcarboxamido))-4-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrimidine;
- (83) 2,4-bis(cyclobutylmethoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (84) 2-cyclobutylmethoxy-4-(6-fluoro-3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (85) 2-cyclobutylmethoxy-4-(5-chloro-3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (86) 2-methylsulfonyl-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (87) 2-cyclobutylmethoxy-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (88) 2-(2,2-dimethylpropyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (89) 2-(2-t-butyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (90) 2-(2-cyclobutyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (91) 2-(n-propyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (92) 2-(n-butyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (93) 2-(sec-butyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (94) 2-(iso-butyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (95) 2-(isopropyloxy)-4-(3-pyridyloxy)-5-(4-chtorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (96) 2-(n-pentyloxy)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (97) 2-cyclopropyloxy-4-(4-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (98) 2,4-bis-(4-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (99) 2-(isobutyloxy)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (100) 2-(cyclopropylmethoxy)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (101) 2-(isopropyloxy)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (102) 2-ethoxy-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (103) 2-(N-pyrrolidinyl)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;

- (104) 2-(N,N',N'-trimethyl-ethylenediamino)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (105) 2-(N-piperidinyl)-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (106) 2-(N-morpholinyl)-ethylenediamino-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (107) 2-dimethylamino-4-(3,4-difluorophenoxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (108) 2-(N-pyrrolidinyl)-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (109) 2-methylsulfonyi-4-(2-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (110) 2-(2-isopropyloxy)-4-(2-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (111) 2-(2-N,N',N'-trimethyl-ethylenediamino)-4-(2-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (112) 2-(2-pyrrolidinyl)-4-(2-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (113) 2-(methylsulfonyl)-4-methoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (114) 2-methoxy-4-(methylsulfonyl)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (115) 2-(3,4-difluorophenyloxy)-4-methoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (116) 2-methoxy-4-(3,4-difluorophenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (117) 2-(3-fluorophenyloxy)-4-methoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (118) 2-methoxy-4-(3-fluorophenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (119) 2-methoxy-4-(2-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (120) 2-(2-pyridyloxy)-4-methoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (121) 2-(5-chloro-3-pyridyloxy)-4-methoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (122) 2-methoxy-4-(5-chloro-3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (123) 2-(3-pyridyloxy)-4-methoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (124) 2-methoxy-4-(3-pyridyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (125) 2-methoxy-4-(4-fluorophenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (126) 2-methoxy-4-(3,5-difluorophenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (127) 2-methoxy-4-(3-cyanophenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (128) 2-(3,4-difluorobenzyloxy)-4-methoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (129) 2-methoxy-4-(3,4-difluorobenzyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (130) 2-(methylsulfonyl)-4-ethoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (131) 2-ethoxy-4-(methylsulfonyl)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (132) 2-(3,4-difluorobenzyloxy)-4-ethoxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (133) 2-ethoxy-4-(3,4-difluorophenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (134) 2-(methylsulfonyl)-4-isopropyloxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;

- (135) 2-isopropyloxy-4-(methylsulfonyl)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidine;
- (136) 2-(3,4-difluorobenzyloxy)-4-isopropyloxy-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (137) 2-isopropyloxy-4-(3,4-difluorophenyloxy)-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (138) 2-(3,4-difluorobenzyloxy)-4-pyrrolidinyl-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (139) 2-(3,4-difluorobenzyloxy)-4-dicthylamino-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (140) 2-(3,4-difluorobenzyloxy)-4-dimethylamino-5-(4-chlorophenyl)-6-(2,4-dichlorophenyl) pyrimidine;
- (141) 2-(3,4-difluorophenoxy)-4-methoxy-5-(4-fluorophenyl)-6-[2, 4-dichlorophenyl]pyrimidine;
- (142) 2-(3,4-difluorophenoxy)-4-methoxy-5-(4-methoxyphenyl)-6-[2, 4-dichlorophenyl]pyrimidine;
- (143) 2-(3,4-difluorophenoxy)-4-methoxy-5-(4-trifluoromethylphenyl)-6-[2, 4-dichlorophenyl] pyrimidine;
- (144) 2-(3,4-difluorophenoxy)-4-methoxy-5-(3-chlorophenyl)-6-[2, 4-dichlorophenyl]pyrimidine; and
- (145) 2-(3,4-difluorophenoxy)-4-methoxy-5-(3-methoxyphenyl)-6-[2, 4-dichlorophenyl]pyrimidine, or a pharmaceutically acceptable salt thereof.

Claim 27. (new) The method according to Claim 11, wherein in the compound of structural formula I,

R1 is selected from:

- (1) C₁₋₆alkyl,
- (2) -OH,
- (3) -OC1-6alkyl, unsubstituted or substituted with one to three R^c substituents,
- (4) cycloalkyloxy-, unsubstituted or substituted with one to three Rc substituents,
- (5) cycloalkyl-C₁-4alkyloxy-, unsubstituted or substituted with one to three RC substituents.
- (6) cycloheteroalkyloxy-, unsubstituted or substituted with one to three RC substituents,
- (7) cycloheteroalkyl-C₁₋₄ alkyloxy, unsubstituted or substituted with one to three Rc substituents.
- (8) phenyloxy, unsubstituted or substituted with one to three Rc substituents,
- (9) heteroaryloxy, unsubstituted or substituted with one to three RC substituents,
- (10) phenyl-C1-4alkyloxy, unsubstituted or substituted with one to three RC substituents,
- (11) heteroaryl-C1-4alkyloxy, unsubstituted or substituted with one to three Rc substituents,

- (12) -NRaRb,
- (13) -NRbC(O)Ra,
- (14) -CO₂H,
- (15) C1-6alkyloxycarbonyl-, unsubstituted or substituted with one to three R^c substituents,
- (16) cycloalkyloxycarbonyl-, unsubstituted or substituted with one to three RC substituents.
- (17) cycloalkyl-C₁-4alkyloxycarbonyl-, unsubstituted or substituted with one to three R^c substituents,
- (18) phenyloxycarbonyl, unsubstituted or substituted with one to three Rc substituents,
- (19) heteroaryloxycarbonyl, unsubstituted or substituted with one to three Rc substituents,
- (20) phenyl-C₁-4alkyloxycarbonyl, unsubstituted or substituted with one to three Rc substituents,
- (21) heteroaryl-C₁-4alkyloxycarbonyl, unsubstituted or substituted with one to three RC substituents,
- (22) -C(O)NRaRb,
- (23) cyano,
- (24) -SO₂C₁₋₆alkyl, unsubstituted or substituted with one to three R^c substituents; and provided that R¹ is not -NH₂;

or a pharmaceutically acceptable salt thereof.

Claim 28. (new) The method according to Claim 27, wherein, in the compound of structural formula I:

Ra and Rb are each selected from:

- (1) hydrogen,
- (2) C1-6alkyl, unsubstituted or substituted with one to three Rc substituents,
- (3) cycloalkyl, unsubstituted or substituted with one to three Rc substituents,
- (4) cycloalkyl-C1-4alkyl, unsubstituted or substituted with one to three Rc substituents,
- (5) phenyl, unsubstituted or substituted with one to three Rc substituents,
- (6) heteroaryl, unsubstituted or substituted with one to three Rc substituents,
- (7) phenyl-C₁₋₄alkyl, unsubstituted or substituted with one to three Rc substituents, or
- (8) heteroaryl-C₁-4alkyl, unsubstituted or substituted with one to three R^c substituents, or when bonded to nitrogen, R^a and R^b together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-R^d, unsubstituted or substituted on carbon with one to three R^c substitutents;

or a pharmaceutically acceptable salts thereof.

AUG-28-2006 17:04 P.27

> Serial No.: 10/527,561 Case No.: 21204P 26

Page No .:

Claim 29. (new) The method according to Claim 28, wherein, in the compound according to Claim 1.

R1 is selected from:

- (1) C₁₋₆alkyl,
- (2) -OC1-6alkyl, unsubstituted or substituted with one to three RC substituents,
- (3) C4-7cycloalkyloxy-, unsubstituted or substituted with one to two Rc substituents,
- (4) cycloalkyl-C1-3alkyloxy-, unsubstituted or substituted with one to two RC substituents,
- (5) phenyloxy, unsubstituted or substituted with one to two RC substituents.
- (6) pyridyloxy, unsubstituted or substituted with one to two RC substituents,
- (7) phenyl-C1-3alkyloxy, unsubstituted or substituted with one to two RC substituents,
- (8) pyridyl-C1-3alkyloxy, unsubstituted or substituted with one to two RC substituents,
- (9) -NRaRb, wherein:

Ra is selected from:

- (a) C1-6alkyl, unsubstituted or substituted with one to three Rc substituents,
- (b) cycloalkyl, unsubstituted or substituted with one to two RC substituents,
- (c) cycloalkyl-C1_4alkyl, unsubstituted or substituted with one to two RC substituents,
- (d) phenyl, unsubstituted or substituted with one to two Rc substituents,
- heteroaryl, unsubstituted or substituted with one to two RC substituents, (e)
- benzyl, unsubstituted or substituted with one to two RC substituents, (f)R^b is selected from:
- (a) hydrogen,
- C1-6alkyl, unsubstituted or substituted with one to three Rc substituents, or Ra and Rb together with the nitrogen atom to which they are attached form a bridged or unbridged heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-Rd, unsubstituted or substituted on carbon with one to two Rc substitutents,

(10) -NRbC(O)Ra, wherein:

Ra is selected from:

- (a) hydrogen.
- (b) C1-6alkyl, unsubstituted or substituted with one to three Rc substituents,
- cycloalkyl, unsubstituted or substituted with one to two Rc substituents, (c)
- (d) cycloalkyl-C1_4alkyl, unsubstituted or substituted with one to two Rc substituents,
- (c) phenyl, unsubstituted or substituted with one to two RC substituents,

- (f) pyridyl, unsubstituted or substituted with one to three Rc substituents,
- (g) benzyl, unsubstituted or substituted with one to two Rc substituents.
- (h) pyridylmethyl-, unsubstituted or substituted with one to three Rc substituents,

Rb is selected from:

- (a) hydrogen,
- (b) C₁₋₆alkyl, unsubstituted or substituted with one to three R^c substituents,
- (11) -CO₂H,
- (12) C1-6alkyloxycarbonyl-, unsubstituted or substituted with one to three RC substituents,
- (13) -C(O)NRaRb, wherein;

Ra is selected from:

- (a) hydrogen,
- (b) C₁₋₆alkyl, unsubstituted or substituted with one to three R^c substituents,

Rb is selected from:

- (a) hydrogen, and
- (b) C₁₋₆alkyl, unsubstituted or substituted with one to three R^c substituents.
- (14) cyano
- (15) -SC1-6alkyl, unsubstituted or substituted with one to three Rc substituents, and
- (16) -SO₂C₁-6alkyl, unsubstituted or substituted with one to three R^c substituents; each R^c is independently selected from:
 - (1) C₁₋₃alkyl,
 - (2) hydroxy,
 - (3) -OC1-3alkyl,
 - (4) halogen,
 - (5) -SCH3,
 - (6) -SH,
 - (7) -NRdRe
 - (8) $-C(O)C_{1-3}$ alkyl
 - (9) -CO2C1-3alkyl,
 - (10) -CO₂H,
 - (11) -CN,
 - (12) -CF₃,
 - (13) -OCF3,
 - (14) cycloheteroalkyl,
 - (15) phenyl,
 - (16) benzyl, and
 - (17) pyridyl;

Serial No.: 10/527,561 Case No.: 21204P

Page No.: 28

or a pharmaceutically acceptable salts thereof.

Claim 30. (new) The method according to Claim 28, wherein, in the compound according to Claim 1, R² is selected from:

- (1) hydrogen,
- (2) C₁₋₆alkyl,
- (3) –OH,
- (4) -OC1-6alkyl, unsubstituted or substituted with one to three RC substituents,
- (5) cycloalkyloxy-, unsubstituted or substituted with one to three RC substituents,
- (6) cycloalkyl-C1-4alkyloxy-, unsubstituted or substituted with one to three RC substituents.
- (7) cycloheteroalkyloxy-, unsubstituted or substituted with one to three RC substituents,
- (8) cycloheteroalkyl-C1-4 alkyloxy, unsubstituted or substituted with one to three RC substituents,
- (9) phenyloxy, unsubstituted or substituted with one to three R^c substituents,
- (10) heteroaryloxy, unsubstituted or substituted with one to three RC substituents,
- (11) phenyl-C1_4alkyloxy, unsubstituted or substituted with one to three RC substituents,
- (12) heteroaryl-C₁-4alkyloxy, unsubstituted or substituted with one to three R^c substituents,
- (13) -NRaRb.
- (14) -NRbC(O)Ra,
- (15) -CO₂H,
- (16) C1-6alkyloxycarbonyl-, unsubstituted or substituted with one to three RC substituents,
- (17) cycloalkyloxycarbonyl-, unsubstituted or substituted with one to three RC substituents,
- (18) cycloalkyl-C₁₋₄alkyloxycarbonyl-, unsubstituted or substituted with one to three R^c substituents,
- (19) phenyloxycarbonyl, unsubstituted or substituted with one to three Rc substituents,
- (20) heteroaryloxycarbonyl, unsubstituted or substituted with one to three RC substituents,
- (21) phenyl-C1_4alkyloxycarbonyl, unsubstituted or substituted with one to three RC substituents,
- (22) heteroaryl-C₁-4alkyloxycarbonyl, unsubstituted or substituted with one to three RC substituents,
- (23) -C(O)NRaRb,
- (24) cyano,
- (25) -SC1-6alkyl, unsubstituted or substituted with one to three Rc substituents, and
- (26) -SO₂C₁-6alkyl, unsubstituted or substituted with one to three R^c substituents, or a pharmaceutically acceptable salts thereof.

Claim 31. (new) The method according to Claim 27, wherein, in the compound of formula I: R1 is selected from:

- (1) methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert.-butyl, n-pentyl, or 2,2-dimethylpropyloxy,
- (2) methoxy, ethyloxy, isopropyloxy, n-butyloxy, sec-butyloxy, isobutyloxy, tert.-butyloxy, n-pentyloxy, or 2,2-dimethylpropyloxy, unsubstituted or substituted with one to three halo, hydroxy, or methoxy substituents,
- (3) cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, or cycloheptyloxy,
- (4) cyclopropylmethoxy, cyclobutylmethoxy, cyclopentylmethoxy, cyclohexylmethoxy, or cycloheptylmethoxy,
- (5) 4-fluorophenyloxy, 4-chlorophenyloxy, 4-methoxyphenyloxy, 3-fluorophenyloxy, 3-chlorophenyloxy, 3,4-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy,
- (6) 4-pyridyloxy, 3-pyridyloxy, 6-chloro-3-pyridyloxy, or 5-chloro-3-pyridyloxy,
- (7) benzyloxy, 3-fluorobenzyloxy, 3-chlorobenzyloxy, 4-fluorobenzyloxy, 4-chlorobenzyloxy, 3,4-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-dichlorobenzyloxy, 2,4-fluorobenzyloxy, 2,4-dichlorobenzyloxy, alpha-methyl-4-fluorobenzyloxy, or alpha,alpha-dimethyl-4-chlorobenzyloxy,
- (8) 2-pyridylmethyloxy 3,-pyridylmethyloxy, or 4-pyridylmethyloxy,
- (9) N-methylamino, N,N-dimethyamino, N,N-diisopropylamino, or N(CH₃)CH₂CH₂N(CH₃)₂, or N-containing heterocycloalkyl bonded via nitrogen selected from: morpholinyl, thiomorpholinyl, pyrrolidinyl, piperidinyl, and [2.2.1]azabicycloheptyl,
- (10) -NHCORa wherein Ra is selected from:
 - (a) hydrogen,
 - (b) C₁₋₄alkyl,
 - (c) C4-6cycloalkyl, and
 - (d) phenyl, 4-fluorophenyl, 4-chlorophenyl, 3,4-difluorophenyl, or 3,4-dichlorophenyl,
- (11) -CO₂H,
- (12) $-C(O)NH_2$,
- (13) -CN, and
- (14) -SO₂CH₃:

R² is selected from:

- (1) hydrogen,
- (2) methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert.-butyl, n-pentyl, or 2,2-dimethylpropyloxy,

- (3) –OH,
- (4) methoxy, ethyloxy, isopropyloxy, n-butyloxy, sec-butyloxy, isobutyloxy, tert.-butyloxy, n-pentyloxy, or 2,2-dimethylpropyloxy, unsubstituted or substituted with one to three halo, hydroxy, or methoxy substituents,
- (5) cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, or cycloheptyloxy,
- (6) cyclopropylmethoxy, cyclobutylmethoxy, cyclopentylmethoxy, cyclohexylmethoxy, or cycloheptylmethoxy,
- (7) 4-fluorophenyloxy, 4-chlorophenyloxy, 3-fluorophenyloxy, 3-chlorophenyloxy, 3-cyanophenyloxy, 3,4-difluorophenyloxy, 3,5-difluorophenyloxy, 3,5-difluorophenyloxy, or phenyloxy,
- (8) benzyloxy, 3-fluorobenzyloxy, 3-chlorobenzyloxy, 4-fluorobenzyloxy, 4-chlorobenzyloxy, 3,4-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-difluorobenzyloxy, 3,5-dichlorobenzyloxy, 2,4-fluorobenzyloxy, or 2,4-dichlorobenzyloxy,
- (9) 4-pyridyloxy, 3-pyridyloxy, 6-chloro-3-pyridyloxy, or 5-chloro-3-pyridyloxy,
- (10) amino, N-methylamino, N-cthylamino, N,N-dimethylamino, N,N-diethylamino, N,N-disopropylamino, or N-containing heterocycloalkyl bonded via nitrogen selected from: pyrrolidinyl, and piperidinyl,
- (11) -NHCORa wherein Ra is selected from:
 - (a) hydrogen, and
 - (b) C₁₋₄alkyl,
- (12) -CN, and
- (13) -SO₂CH₃;

R3 and R4 are each independently selected from:

- (1) 4-chlorophenyl,
- (2) 4-methoxyphenyl,
- (3) 4-fluorophenyl.
- (4) 4-trifluoromethylphenyl,
- (5) 3-chlorophenyi,
- (6) 3-methoxyphenyl,
- (7) 2,4-dichlorophenyl, and
- (8) 2-chloro-4-methylthiophenyl;

or a pharmaceutically acceptable salts thereof.

Claim 32. (new) The method according to Claim 31, wherein, in the compound of formula I: R3 is 4-chlorophenyl and R4 is 2,4-dichlorophenyl, or a pharmaceutically acceptable salt thereof.